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VOL. VI. No. 7. JUNE, 1913.

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TRANSACTIONS

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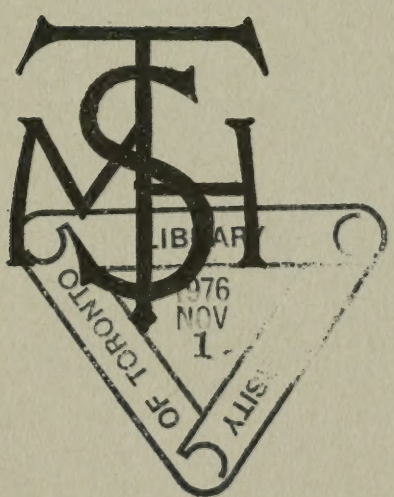
OF

THE SOCIETY OF TROPICAL MEDICINE AND HYGIENE



London:
SOCIETY OF TROPICAL MEDICINE AND HYGIENE
11 CHANDOS STREET, CAVENDISH SQUARE, W. 1

TRANSACTIONS
OF THE
SOCIETY OF TROPICAL MEDICINE AND HYGIENE.

JUNE, 1913.
VOLUME VI. No. 7.

Proceedings of a Meeting of the Society on Friday, May 16th, 1913, SIR R. HAVELOCK CHARLES, G.V.C.O., *Vice-President*, in the Chair.

PHLEBOTOMUS FEVER AND DENGUE.

BY LIEUT.-COL. C. BIRT, R.A.M.C.

After an incubation period of from four to seven days, phlebotomus or sandfly fever is ushered in with violent headache, chiefly confined to the forehead and back of the eyes; pains in the calves of the legs; discomfort in the epigastrium; and stiffness of most of the muscles of the body: the face is deeply flushed and the features are swollen; the conjunctivæ are injected; vomiting occurs in a quarter of the attacks, and diarrhœa almost as frequently, but constipation is noted in the majority of instances; the temperature rises rapidly to 101° F. to 103° F., and falls gradually to the normal level on the third or fourth day; the pulse remains slow throughout the illness; leucopenia, with a relative decrease in the polynuclears, is an almost constant sign; there is considerable debility during convalescence; in an epidemic, more than 90 per cent. of the cases are first attacks, hence a high degree of immunity is afforded after recovery.

This fever is accurately described in PYM'S *Bulam Fever*, in W. BURNETT'S *A Practical Account of Mediterranean Fever*, and in J. HENNAN'S *Medical Topography*, which were published between the years 1814 and 1830. So exact were the observations of these early physicians that the absence of leucocytosis did not escape them.

Bleeding was the universal remedy at that time, and in 1816, Dr. SKEY, quoted by HENNAN, remarked that it did not often happen that the blood of patients suffering from the Malta summer febricula had a buffy appearance; he noted it once only in 28 cases. Also, in 1822, LIGHTBODY noticed that the buffy coat was absent during the summer, in the sandfly season, but that it was observed in the autumn, when yellow fever was prevalent at Malta. There is generally an initial leucocytosis in yellow fever.

The Army Medical Reports date from 1817, and the Statistical Reports on the Health of the Navy from 1830. We meet with excellent clinical pictures of sandfly fever in these volumes, and we learn how widely prevalent it was during the summer months throughout the whole Mediterranean area, including Gibraltar, Malta, the Ionian Islands, Greece, Cyprus, Crete, Asia Minor, and Egypt.

In 1905, TAUSSIG[1] contributed a masterly article to the *Wiener klinische Wochenschrift* on the short fever which breaks out every summer among the Austrian troops stationed on the Adriatic coast in Bosnia and Herzegovina. He adduced epidemiological evidence that the phlebotomus, a figure of which he gave, should be regarded as the agent in the transmission of the disease. Our Indian investigators were thus forestalled, though MCCARRISON stated in a paper on a kindred ailment in Chitral, which he had studied in 1903 and 1904, inserted in the *Indian Medical Gazette* of 1906, "with regard to suctorial insects, sandflies are those most likely to be implicated. Their appearance corresponds in a striking way with the appearance of the disease, and the fact that they are not found where the disease does not prevail may be more than a coincidence. Experiments in my hands have, however, failed to throw any light on this point. The very great difficulties in working with sandflies may be responsible for this lack of result." And further on, "the use of sandfly and mosquito-proof curtains is also essential, as much for the sake of comfort as for the possible protection which may be afforded against the disease." FOOKS, writing in the *Indian Medical Gazette* of 1908 and 1910 of an outbreak of about 100 cases of a similar fever in 1899, at Landi Kotal, a frontier post west of Peshawar, stated that he thought that sandflies were the means of conveying the infection, since there were no mosquitoes, but the sandflies were abundant. His opinion was confirmed by a study of another epidemic at Sialkot in 1907

In the year 1908, DOERR[2] announced the results of his experiments on the infectivity of the blood of the Dalmatian summer fever, and on the mode of the transmission of the virus by the phlebotomus. Since then the closely related ailments in Malta have been investigated in a similar manner. TEDESCHI and NAPOLITANI[3] have made a similar enquiry into the nature of the Italian "summer influenza." KILROY[4] has put to the test of experiment the causation of the fever as it occurs in Crete.

On combining the successful experimental results, it is found that:—

(1) The subcutaneous injection of blood or serum withdrawn during the first twenty-four hours of the patient's illness caused fever 19 times.

(2) Inoculation with the filtrate obtained by passing the diluted blood through a porcelain candle which retained the *micrococcus melitensis*, excited the disease 14 times.

(3) Feeding experiments with infected sandflies were successful on 21 occasions.

This evidence is sufficient to shew that the fever is specific, and that it is caused by a filter-passing virus, which circulates in the blood during the first day of the illness, and that it is conveyed by the phlebotomus.

The movements of our soldiers and sailors have formed an experiment on a vast scale. Every year for the last century hundreds of susceptible subjects have been transported to localities where phlebotomi abound, and the number of cases of fever which have arisen after their exposure to the bites of these insects has been registered with great precision. We learn that a large proportion of our soldiers and sailors was attacked with this fever during their first summer of residence in phlebotomus-haunted places; sometimes as many as 55 per cent. of the new arrivals have been seized.

On the other hand, the naval and military forces which have been despatched to tropical and sub-tropical parts where the sandfly does not exist have been exempt from this infection; for instance, in Bermuda, of which the writer has personal knowledge, the phlebotomus is not found, but culex and stegomyia are abundant; "summer influenza" is unknown, although epidemics of dengue and yellow fever have broken out at rare intervals in times past.

When examined with the aid of a pocket lens, a phlebotomus is immediately recognised by its form and its very thick hairy coating,

which obscures all the fine details of its structure. On removal of this dense clothing, slender microscopical differences may be observed in the venation of the wings, the length of the segments of the palps, the number and arrangement of the bristles or spines on the claspers, etc., on which entomologists base a classification, but up to the present there has been little agreement amongst them ; a species has been given more than one name, not only by different entomologists but sometimes by the same.

GRASSI[5] has studied the life-history of the phlebotomus in Italy, and MARETT[6] in Malta. It breeds in caves and in the interior of rubble-walls. The eggs hatch in six to nine days after being laid; the larval stage lasts about eight weeks, and as pupæ they exist fixed in crevices in fragments of stone for a fortnight. These flies survive in captivity about ten days only, hence great difficulties are encountered in tracing their history. The phlebotomus is widely scattered throughout the tropical and sub-tropical world, and sandfly fever is almost as broadly expanded.

FRANCA[7] states that the phlebotomus occurs at Collares on the coast of Portugal, north of the mouth of the Tagus, in the months of August to October, and reports that sandfly fever prevails. In the *Statistical Report on the Health of the Navy* for 1833 we read of an outbreak of 285 cases of summer febricula in H.M. ships anchored in the Tagus.

In Gibraltar the phlebotomus is indigenous. In 1804 sandfly fever was studied by PYM, and there have been annual epidemics ever since, though of recent years the number of cases has been decreasing.

The existence of phlebotomus and of the fever in Corsica has been made known recently by LEGER and SEGUINAUD.[8]

LANGERON[9] finds that the phlebotomus is scattered throughout the south of France.

The sandfly is distributed through the whole of Italy, and is abundant in Rome, Naples and Venice. Numerous writers report the prevalence of the infection in all parts. TEDESCHI and NAPOLITANI have made extensive researches in the ætiology of the " summer influenza " of Italy.

In Sicily, GABBI[10] has reported the occurrence of the fever at Catania, Palermo and Partenico. CASTRO states that it breaks out every year among the troops in Milazzo. The writer captured the phlebotomus at Taormina. They are abundant in places where the disease prevails.

In Malta the preventive measures arising from the recognition of the transmitting agent have been effectual in reducing the incidence of sandfly fever. In 1909 there were 253 attacks registered among the British troops; they fell to 124 in the following year; in 1911 there were 125 cases, and last year, I believe, there was a further reduction.

The Ionian Islands—Corfu, Paxo, Santa Maura, Cephalonia, Ithaca, Zante and Cerigo—were occupied by the British during the first half of last century. Every year summer epidemics of this fever are recorded. In 1828, at Santa Maura, the epidemic began in June and ended in November, but not before almost every individual had been attacked.

Doerr and Russ[11] have continued their researches on the fever in Bosnia and Herzogovina, of which Franz and Kolar[12] have made a clinical study. According to these authors the disease is prevalent in the Balkans. Professor Leon[13] announces that he has captured the phlebotomus in Roumania, and Gallio Valerio[14] and de Jongh have found it north of the Alps in Canton Waadt, Switzerland.

Aravandinos[15] states that these flies are common in Greece. He has observed the occurrence of phlebotomus fever in Athens. In the *Naval Reports* it is seen that cases originate at Platea and throughout the Mediterranean generally, including the Riviera.

At Crete, Fleet-Surgeon Kilroy and Surgeon Adshead studied the infection experimentally. Miorcec and Laplanche[16] state that more than half the detachment of 200 French troops were attacked in July and August, 1910.

Sandfly fever was very prevalent among the British troops at Cyprus during the early years of the occupation. A few cases are still recorded annually.

Mühlens[17] announces the presence of the phlebotomus and of the malady at Jaffa and Jerusalem. In 1864 Chaplin[18] recognised this infection in Jerusalem, and distinguished it from malaria.

The fever is endemic in Asia Minor. The crews of our ships suffer when they are anchored off the coast.

From 100 to 300 attacks of sandfly fever occur among the British troops quartered in Egypt every year. Dr. Sandwith[19] has observed cases in Cairo. Phillips[20] and Wakeling[21] also report instances in Cairo. Balfour[22] has recognised the ailment at Khartoum. The phlebotomus is found throughout Egypt and the Soudan.

PRESSAT[23] states that the sandfly has been captured in Arabia and along the Red Sea.

Extensive epidemics of sandfly fever have prevailed among the British garrison of Aden, where the writer himself experienced an attack.

The crews of our ships in the Persian Gulf are liable to outbreaks of this fever.

India is the country in which cases of sandfly fever are most numerous. Reference has been made already to MCCARRISON'S and FOOK'S accounts of the disease at Chitral, Landi Kotal and Sialkot. WIMBERLEY[24] described an epidemic which prevailed at Nowshera in 1910. WALL[25] has given an account of the Chitral outbreaks of 1909 and 1910. C. H. HALE[26] reported an epidemic in Kamptee in 1911; he found that camphor is effective in driving away sandflies. ROBINSON and BLACKHAM[27] state that the malady caused 848 admissions to hospital among the British troops of the Peshawar Division in 1911. TAYLOR and KHAN[28] observed 161 attacks in the Indian troops at the frontier post Parachinar during the months of June to September, 1912. In the *Annual Report of the Sanitary Commissioner with the Government of India for the year 1910*, published in 1912, the total number of cases of sandfly fever recorded among the British and Indian troops is 1,058. It is doubted whether the great importance of this disease as a cause of disability of our troops has yet been widely realised; it is probable that there were some four or five thousand attacks in all. The *Army Medical Report* of 1911 gives 1,393 admissions on account of sandfly fever among the British troops alone stationed in India in 1911.

The phlebotomus is abundant in Ceylon, and our troops have suffered from the fever.

About 70 or 80 cases of this ailment are recorded each year in the returns of our troops stationed at Hong Kong and the Straits Settlements.

At Tientsin and Pekin, in 1911, 45 cases occurred in the British garrison when sandflies were most numerous.

The sandfly is widely distributed in the French possessions in Africa. LANGERON reported its existence on the coast of Tunis. FOLEY and LEDUC[29] state that it is common in southern Algeria. ROUBAUD[30] finds that it is extended throughout West Africa, and is abundant in Timbuctoo.

In 1903, THEOBALD[31] wrote that phlebotomi occur in most collections of flies from West and Central Africa. It has been captured in Uganda. NEWSTEAD[32] says that it inhabits the Soudan, British Central and West Africa and Rhodesia. MANTEUFEL[33] has reported the existence of the phlebotomus and of the infection in German East Africa. At Zanzibar, in the year 1911, 17 of the crew H.M.S. "Pandora" were attacked with sandfly fever.

In North America the phlebotomus has been caught in Maryland.[34]

In Central America it has been reported in Guatemala. MCGIBBON[35] published an account of a short summer fever which prevailed at San Fernando on the west coast of Mexico in 1911. No rashes of any sort were observed; it is probable that the infection was phlebotomus fever.

According to the observations of LUTZ and NEIVA[36] the phlebotomus is broadly scattered throughout Brazil.

Dengue breaks out in epidemics which are far more explosive in character than are those of sandfly fever. The infection courses swiftly through a community, until almost all susceptible people have been attacked. In a few weeks its energy will have been expended. The rashes which occur in about 70 per cent. of the cases, and the greater severity of the pains, mark off this disease from sandfly fever, in the Malta, Italian and Chitral epidemics, of which their absence has been noted.

The infections may occur in the same locality. At Aden, in 1893, the summer outbreak of phlebotomus fever was followed by one of dengue in the autumn. No immunity was afforded by the former infection against the latter; whole families were seized; papular or urticarial rashes broke out in most cases. The writer's experience of his own attack at that time was that the joints were more painful than in the phlebotomus infection, and that the initial rash was accompanied with itching of the palms and soles. Dengue has often visited Aden, and is well known to the native inhabitants, who call it "father of the knees." In the *Naval Medical Report of 1871* we read of the devastations dengue caused in Aden in that year. The garrison and the whole population, European and native, were seized indiscriminately, so that in a few days' time all Aden, civil and military, was *hors de combat*. Swollen glands were a feature of the outbreak.

In Gibraltar and Malta dengue has appeared among the troops in the autumn at the end of the sandfly fever epidemic. The occurrence of rashes and breakbone pains, it is stated, were prominent symptoms, hence there was no confusion in determining the infections.

In Greece, ARAVANDINOS says that dengue arises every few years in epidemic form along the coast, and that it can be distinguished readily from sandfly fever, to which visitors to Greece are liable.

Many excellent accounts of dengue have been published; notably that of Dr. SANDWITH[37] of the infection in Egypt, and that of Fleet-Surgeon BASSETT-SMITH[38] of outbreaks in Bombay. There is considerable variety in the character of the symptoms observed in the various epidemics. BASSETT-SMITH remarked on the absence of severe bone and joint pains and of enlarged lymph glands. In an outbreak among our troops at Stanger, Natal, reported by BEVERIDGE,[39] many of the cases of which were seen by the writer, the swelling of the lymphatic glands was noted in 99 per cent. of the 325 cases, along with the classical signs and symptoms of the infection.

Aberrant cases of dengue, and they occur in every epidemic, closely resemble sandfly fever. After a similar incubation period, there is the same intense frontal headache, flushed face, injected and tender eyes, pains in the body and limbs, slow pulse, and leucopenia. STITT[40] found that the average leucocyte count in 100 cases of dengue was 3,200. Moreover, the late eosinophilia observed by BALFOUR[41] in Khartoum, by HARNETT[42] in Calcutta, and by others, also occurs in sandfly fever, so that the infections cannot be separated by microscopical examination of the blood.

H. GRAHAM,[43] of Beyrout, was the first to investigate dengue experimentally. After feeding *culex fatigans* on dengue patients, he caused them to bite susceptible people residing in places where the disease was absent. He thus transmitted the infection to six persons. He also induced the disease by inoculating a man with an emulsion of the salivary glands of an infected culex.

In 1904, CARPENTER and SUTTON[44] obtained successful results with culex and stegomyia at the Isthmus of Panama.

In 1906, ASHBURN and CRAIG[45] ascertained that the blood of dengue patients was infective, and that the virus passed through a filter which was impervious to the *micrcoccus melitensis*.

Summarising the successful experiments, we find that—

Inoculation with the blood of dengue sufferers caused dengue eight times.

Inoculation with filtered infective blood induced the disease twice.

Inoculation with the salivary glands of an infected culex gave rise to dengue once.

Infection has been conveyed by infected culices eight times.

Infection has been conveyed by infected stegomyia once.

There are considerable differences in the infectivity of the virus in sandfly fever and dengue. Blood abstracted after the first twenty-four hours in the course of sandfly fever no longer can excite the disease. It has failed to do so in every attempt (five experiments made). The blood of dengue patients with which the successful inoculations were performed, was drawn off on the second to the fifth days of the disease.

Whereas phlebotomi are not capable of transmitting sandfly fever until six days after feeding on a sandfly fever patient who is in the first day of his illness, dengue has been conveyed by mosquitoes immediately after their meal of dengue blood; nevertheless the virus survives in them, for they have conveyed the disease 8-27 days after feeding on a dengue sufferer.

Graham protected families from dengue by means of mosquito curtains. E. H. Ross[46] extinguished epidemics of dengue which had been of yearly occurrence in Port Said by exterminating the mosquitoes. Stitt prevented the spread of infection from 200 dengue patients to others in the same ward by enclosing the former in mosquito-proof wire cages.

The evidence is accumulating that the stegomyia is an agent in the propagation of dengue. Legendre[47] concludes from a study of an extensive epidemic of dengue at Hanoi in 1910, that the stegomyia was the responsible vector, since the outbreak was coincident with a great increase in the number of these mosquitoes, while other species were few. The arrest of the epidemic was marked by a diminution in the stegomyiæ and an increase in the other mosquitoes. Davidson[48] remarks that stegomyiæ were everywhere during the recent outbreak of dengue at Brisbane. Lalor,[49] cited by Surgeon-General Lukis, believes that the short fevers which are prevalent at Rangoon are conveyed by stegomyia.

That there is some connection between epidemics of dengue and

yellow fever has long been noted. In Bermuda,[50] in the year 1863, there was an autumn outbreak of dengue, which was followed in the next summer by a disastrous epidemic of yellow fever in which over 3,000 out of a population of 11,450 persons were seized. The epidemics were connected by the occurrence of atypical febrile cases in the interval. In 1881 at Malta there was an outbreak of dengue during the autumn, and 69 cases of yellow fever then occurred among the troops.

There is a close resemblance between the dengue, sandfly and yellow fever infections; they are all caused by some virus which circulates in the blood, and is capable of passing through a filter which retains bacteria; the onset of the fever is similar in many instances, and during the first forty-eight hours of the illness it may be impossible to distinguish between the infections; even later a diagnosis on clinical grounds may be unattainable, for atypical cases of dengue and yellow fever may bear every likeness to phlebotomus fever. Hence too great stress should not be laid on the symptoms of individual patients during the course of an epidemic; it is the general type of case which will give the name to the outbreak.

We now come to the consideration of those fevers which Rogers[51] has described as "sporadic seven-day fever simulating dengue." The name is hardly suitable, perhaps, for of the 206 cases on which his report is based, in 66 only was the duration of the pyrexia seven days; in 79 it was six days, and in the rest it varied from three to more than eight days. The leucopenia, slow pulse, and rashes cause little hesitation in identifying this disease with dengue. From the blood of six patients, however, a bacillus bearing many of the characters of the *B. typhosus* was isolated, but since 1907, the date of the report, there has been no more positive evidence of the bacterial nature of the fever. Megaw,[52] who himself was a sufferer, believes that it is a mosquito-borne malady. Fleet-Surgeon Clayton[53] has given powerful reasons for the belief that the so-called seven-day fever of eastern ports is conveyed by mosquitoes. Butler[54] remarks that many cases which occurred in the 1911 Brisbane dengue epidemic conformed to this type.

In Jamaica and Bermuda of recent years blood cultures have been employed in the investigation of atypical febrile diseases which have appeared among our troops, in addition to the usual microscopical and serological examinations: the upshot has been, that six or a dozen or

more cases occur every year in which the blood is sterile, and the microscopical and serum examinations are negative. In both islands culices and stegomyiæ are abundant and phlebotomi are absent. It is probable that such febrile attacks are caused by these mosquitoes.

In 1909 the writer was sent to Malta to look for the fever investigated by DOERR. He arrived before sandflies had made their appearance, and before the outbreak of phlebotomus fever. In April and the beginning of May six cases came under his notice in which the duration of the pyrexia was from five to ten days. In all of these 5-10 c.c. of blood remained sterile permanently; the serological and microscopical examinations for parasites were negative; leucopenia and a slow pulse were observed in every instance. These cases, therefore, resembled many which occur in dengue epidemics. After the commencement of the sandfly fever season, eight more attacks with pyrexia varying from 5 to 16 days, were investigated, with similar results. The conclusion seems justified that these were mosquito-borne infections. Sporadic cases of yellow fever may occur, and there is no inherent improbability that isolated examples of dengue should arise. The cases of greatest severity appeared in the autumn months when the stegomyiæ were becoming more numerous, and it is not unlikely that they were the transmitting agents. Surgeon-Major MIFSUD, of the Royal Malta Artillery, informed the writer that occasionally he had encountered febrile cases in which bilious vomiting and jaundice were prominent symptoms, suggesting that the stegomyia was the cause.

We should not be content with such terms as "3-day," "7-day," "10-day" fevers, for such expressions are inaccurate, no fever keeps time so precisely; "remittent fever" and "pyrexia of unknown origin" are convenient names to be employed when we are overworked and fatigued. In perusing the literature of fevers we see how much more preoccupied the writers have been with a search for a name than with finding out the cause of a disease. Much energy and ink have been expended on discussing whether a fever is "BRILL'S disease," "WEIL'S disease," yellow fever, "bilious remittent fever," "3-day," "7-day" fever, and so forth, when an appeal to experiment would have answered the question and would have saved lives.

It would be a distinct gain to the cause of public health if infections were designated by their transmitting agency. The names

"rat-flea fever," "louse fevers," "bug fever," "tick fever," "goat-milk fever," "mosquito fevers," bring vividly to the notice of the public their dangerous foes, and we thus educate them in the means to be adopted in the prevention of disease, and enlist their services for their suppression. The question of names appears to be a subject worthy of the consideration of this Society at the present time, for there is now sitting the Joint Committee appointed by the Royal College of Physicians for the purpose of revising the nomenclature of diseases, and an authoritative statement of the opinion of this Society would aid the Committee in that part of their work which refers to tropical diseases.

The practical sanitarian will insist perhaps, in the presence of an epidemic, on the destruction of all blood-sucking insects, and the reduction in the incidence of the fever will prove the value of this measure. But the expense of such a crusade may be prohibitive, and an experimental investigation will then be necessary to narrow down the campaign to the extirpation of those insects or other agencies which alone are responsible for the outbreak.

CONCLUSIONS.

Dengue, phlebotomus and yellow fevers are caused by distinct but closely related kinds of virus.

A fever lasting several days in which the examination of the blood for parasites, by culture, and by serum tests, is negative; characterised by slow pulse, leucopenia, and relative polynuclear decrease; occurring in a locality where mosquitoes are numerous, should be attributed to a virus carried by these flies, although some of the symptoms significant of dengue or yellow fever may be wanting.

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For a synopsis of the genus Phlebotomus, see

SUMMERS. Jour. London School of Trop. Med. 1913. April. Vol. 2. Part 2. pp. 104–116.

For Indian species, see

BRUNETTI. Fauna of British India—Diptera, Nematocera. 1912. pp. 199–216.

For an extended account of the history of Dengue, see

MAHÉ. Dictionnaire Encyclopedique des Sciences Médicales. 1883. Tome 26. pp. 698–738.

DISCUSSION.

Sir HAVELOCK CHARLES: I think we have heard to-night a paper of extreme interest clinically. Most of the meetings of this Society have been bacteriological evenings. This evening is interesting to the sanitarian, and also to the bacteriologist, but especially to the man who stands by the bedside.

Our thanks are undoubtedly due to Lt.-Col. BIRT for the very able paper he has given us. There is no doubt about it that he is of the opinion that dengue and phlebotomus fever are totally different diseases. Major MEGAW holds a different view. Col. BIRT did not traverse Major MEGAW'S report, as I hoped he would have done. There seem to be two schools in this; the unity and the dualist. Col. BIRT is a dualist. We shall see before the evening finishes, when light has been shed upon this a little more, what the opinion of the meeting is.

There is very great difficulty in differentiating these short fevers, especially from commencing malaria and enteric. If you are absolutely sure that it is a case of 7-day fever, or a case of dengue, you can relieve the anxiety of the patient and his friends; that is very valuable for the practitioner. Another point is the differential diagnosis of the 3-day fever, the 7-day fever, and dengue from each other; but as the treatment of all is the same, the diagnosis is more or less of academic interest. That is one way of looking at it, but I do not think it is a good way.

My own experience of these two diseases has been personal and painful. I have suffered in the Punjab from short fever, which was not malaria, and also from dengue in Calcutta. In the Philippine Islands we have heard that convalescence is rapid and uninterrupted, but I did

not recover for months and months, and I still have twinges in my shoulder. That was a true case of dengue. From personal experience I am rather inclined to look upon the two diseases as different.

I should like to ask Dr. SANDWITH if he will kindly tell us his opinion on the matter.

Dr. F. M. SANDWITH: This valuable paper almost reminds me of the eulogy passed by Charles II. upon his chaplain, Isaac Barrow. He called him "an unfair preacher, because he exhausted every topic and left no room for anything new to be said by anyone who came after him!"

I do not mean, of course, to imply that Lt.-Col. BIRT is an unfair writer, but I want to express, in simple language, our indebtedness to him for going so thoroughly into the matter of these fevers.

There is only one thing I can find to criticise. He was kind enough to refer to my name as having observed cases in Cairo and the Sudan. I should like to ask him if he would kindly alter that to Cairo and the rest of Egypt. Phlebotomus fever has been reported from the Sudan, but not by me.

We should like very much indeed to hear from Col. BIRT—it is the province of the after speaker to propose conundrums—if he could tell us how phlebotomus fever is continued. He tells us, as other observers have done, that the insect lives in captivity for ten days. It is such a delicate, miserable-looking creature, so sensitive to the winds of heaven, that it is difficult to believe it would live for very long. I believe we hold the view that the domestic fly can hibernate in winter, and manage to carry on its brood. The domestic fly is a robust, happy sort of herculean creature compared with the phlebotomus. One wonders how the phlebotomus lives to produce offspring, and one wonders also how phlebotomus fever is continued. It has been suggested that the phlebotomus conveys infection to its own progeny, as we know some other insects do. It is obvious that some sort of development must go on in the phlebotomus, if it is only after six days that the phlebotomi prove to be effective.

As you, Sir, have asked for a confession of faith, I should like to state very distinctly that—like yourself an ex-patient, I have had dengue twice, and the other one many times—I think the two diseases are

as absolutely different as chalk is from cheese. I have no faith at all in the supposition that there is any similarity between them whatever. I could better understand some people mistaking dengue and influenza, because dengue and influenza are more similar than dengue and phlebotomus fever.

I am so glad to see that Col. BIRT gives proper praise to Dr. GRAHAM of Beyrout. I do not think I have ever met Dr. GRAHAM, but I was in correspondence with him when he made his discovery in 1902, and I do not think writers on tropical diseases have always quite recognised that he did a similar thing to that which Sir PATRICK MANSON did with regard to malaria, that is to say, he took the dengue poison, whatever it is, up to the hills where there was no dengue, and gave it there to various people, and also he was able to protect other people in the dengue area by mosquito nets. The reason I think he has not met with praise from writers is because he wrote a paper, which he sent to me at the time, in which he made, as it were, two discoveries. First, the insect that conveyed the disease, and the other one was that he found a protozoal cause of it. There he was wrong, and nobody agreed with him about that, and I think people have remembered he was wrong about the protozoon, and have not given him due credit with regard to the mosquito.

I have always been, or I used to be, very much interested in the strong belief that dengue and yellow fever are connected, and curiously enough I have always heard them spoken of in that order. It would be interesting if anyone can tell us of an outbreak of yellow fever followed by dengue.

The explanation is easy if we accept the statement that *stegomyia* is one of the dengue conveyers in addition to *culex fatigans*.

I have had some conversation with Dr. LEONARD ROGERS about his seven-day fever, and have seen some of his charts, and I believe, with Col. BIRT, that ROGERS' "seven-day fever" is what I should call dengue. I looked up some of my own charts of dengue after ROGERS' book was published, and found that some of my own charts of dengue, taken in Cairo, had the saddle-back arrangement which ROGERS thought was specially typical of "seven-day fever."

The last point interesting to me is Col. BIRT'S suggestion that the nomenclature of disease should include some mention of phlebotomus

fever. I would even like to suggest that in the Council of the Society some discussion should take place as to whether it would be possible, through the President, to approach the Royal College of Physicians, to ask them whether there is any member of the Revising Committee who has a special interest in tropical diseases. I forget just now who the Committee are. The last time the nomenclature was revised was in 1906, and I took the liberty then—that was before this Society existed—of conferring with the Secretary, and he allowed me very kindly to make some suggestions, some of which were adopted.

Capt. MARETT: As regards the difference between dengue and sand-fly fever, I have never seen dengue, but I have met patients who have suffered from the disease, and they say the two differ on other points. The only thing I would talk about—and I would sooner be asked questions—is as to the life-history of the fly. If I can say anything on that I shall be very pleased to do so.

Only one question has arisen, and that is as regards the hibernating of the fly, whether they do or do not. In my opinion the female fly invariably dies shortly after laying her eggs. She only lays one batch of eggs, and within twelve hours of laying the eggs she is dead.

As regards infectivity, that has not been worked out, but the popular opinion is—as Dr. SANDWITH mentioned—that the infection is probably carried to the eggs and larvæ and pupæ.

Major CHRISTOPHERS: I should like to ask Col. BIRT regarding the filterability of the virus. He has told us that the virus is filterable, but not to what extent. It seems a very important point. When an insect carrier like the phlebotomus becomes infected after six days, one naturally thinks of some protozoon as the cause of the disease, but it is inconceivable that a protozoon could pass through anything except a very coarse filter. It is rather interesting, therefore, to know how much attention has been devoted to the question of filterability.

Fleet-Surgeon P. W. BASSETT-SMITH: If one looks at the question chiefly from a naval point of view, one is always struck by the enormous number of cases that are entered as simply continued fever in old records.

The work described in the paper of Lt.-Col. BIRT makes one think more about these short fevers, and I hope it will induce other men in the endemic areas to endeavour to try to trace out some of these forms. He has rightly and kindly quoted the work of KILROY as an example in which very complete and careful experiments were carried out as to the transmitability of the virus by the phlebotomus, and such work wants to be carried out more fully.

In going further East, in reference to the question of dengue, the first experience that I had in Bombay was very suggestive indeed. During eighteen months at Bombay, in the naval defence ship, we had three epidemics of fever of this so-called seven-day or dengue type. Personally, I think it was dengue. The cases had definite characteristics: sudden onset of fever, marked rise of temperature, always marked pain, and most of them shewed evidence of rash. These rashes were often not very definite, but they were found to be present if looked for carefully. I may say that in the early series of patients many of the rashes were not recognised, because they were not sufficiently looked for. These cases were very interesting. Every series of men that came out from England, on arrival in the ship, appeared, almost without exception, to contract the disease. On three separate occasions the three drafts were all attacked, there being no immunes among those coming from England. It was not as though the disease was restricted to the ship, for cases were found on the other ships of the flotilla when the men were living quite separately. The disease was not restricted to the hot weather, but the cases occurred in December and March as well as in the middle of the year. Part of the time the ship was in dock where mosquitoes were very abundant, and by these the disease might well have been conveyed. Besides these outbreaks, one finds many others in the Navy where cases of this fever had been found, and often they have been in ships that were for some time in dock and where the possibility of insect infection has been marked. The question of insect infection with dengue can hardly, therefore, be put on one side. The experiments quoted recently of patients suffering from dengue in the Philippines are important; dengue never spreads in a ward provided these patients are treated in mosquito-proof cubicles in the wards. Then another example, which has a great deal of weight in supporting the mosquito origin, is that in the time when SIR RONALD ROSS had

his mosquito campaign in Port Said, dengue was very uncommon. There is no doubt that this disease is one which is widely distributed in tropical and sub-tropical districts. The disease runs, even in endemic centres, rather a typical course. In many cases the true primary and secondary fevers are to be found in Bombay, the Philippines, and, I believe, in Egypt, but the actual charts vary a good deal. The seven-days' fever of ROGERS from my experience is, I believe, a myth.

Dr. J. M. ATKINSON: I think there can be no doubt that the two diseases are quite distinct. In 1902 we had dengue, typical dengue, in Hong Kong. There were hundreds of patients under treatment in the Hospital, all presenting practically the same features. The attack consisted of three days' fever, three days' intermission, and the terminal fever on the sixth or seventh day, accompanied by the distinctive secondary roseolar rash. Eighty per cent. of the patients shewed this secondary eruption. It is quite distinctive in dengue; one does not meet with this secondary rash in any other disease. At the docks, for instance, in Hong Kong, where they employed some 600 to 700 Chinese, no less than 200 to 300 of the Chinese were knocked down with the fever within a few days. I think this tends to shew that the disease is spread more from person to person. In its sudden onset, rapid diffusion, and the great proportion attacked in a community, it very much resembles influenza. You could not imagine 300 persons bitten in one day by an infected mosquito. The way the disease was spread was from person to person in each house. You had a case in a house, and practically everyone in that house who had not had the disease contracted it. At the Civil Hospital, for instance, two-thirds of the Sisters were laid up, and many of the patients contracted the disease. There were very few mosquitoes to be found in the building at that time. It is a disease which occurs in Hong Kong only in the summer months, and I think there can be no doubt that the two diseases, dengue and phlebotomus fever, are quite distinct and separate.

I have never seen a case of phlebotomus fever, and I would like to ask Col. BIRT whether there were any skin eruptions met with in that disease similar to those in dengue.

Sir HAVELOCK CHARLES: I see that on page 245 it mentions "The

subcutaneous injection of blood or serum withdrawn during the first twenty-four hours of the patient's illness caused fever nineteen times."

I should like to ask Lt.-Col. BIRT, what was the total number of cases?

Lt.-Col. BIRT: Every case was successful. No rashes, except the effects of biting insects, have been observed in the Maltese, Cretan, Italian, or Chitral epidemics of phlebotomus fever; but we meet with many cases of dengue in which skin eruptions are absent, and the general pains are not severe. As, moreover, the pyrexia may last three or four days only, such attacks of dengue are indistinguishable from phlebotomus fever.

With regard to the filtration of the virus, in the experiments carried out in Malta, 5 c.c. of blood were mixed with 45 c.c. of sterile physiological salt solution before clotting had taken place. The mixture was placed immediately in a Cobbett's filter fitted with a "Chamberland F. candle controllé." Filtration was conducted very slowly under the pressure of gravity only, at a temperature of 78° F. Twenty-four hours elapsed before 20 c.c. of filtrate had collected. The filtrate contained no microscopical elements, and was sterile on culture. The reliability of the candle was tested, before and after use, with emulsions of the *M. melitensis*, which was retained on both occasions, hence no protozoa were present in the filtrate.

Though it has not been ascertained with certainty how the virus of phlebotomus fever is preserved during the winter, and how the epidemics of phlebotomus fever are bridged over, DOERR has adduced evidence that there is hereditary transmission of the virus from phlebotomus to ovum and larvæ, and thence to the mature fly. The question could be answered by emulsifying the ova of infected phlebotomi, filtering the emulsion through a porcelain candle, and injecting the filtrate into a susceptible subject.

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43 HUMBERSTONE ROAD, LEICESTER
1951